Amendments to the Specification:

Please enter the substitute Sequence Listing into the specification in accordance with 37 C.F.R. § 1.825.

Please amend the specification as follows:

On page 4, amend the third paragraph as follows:

In WO 98/39031, Rice et al. disclosed authentic HCV genome RNA sequences, in particular containing: a) the highly conserved 5'-terminal sequence "GCCAGCC" (SEQ ID NO. 26); b) the HCV polyprotein coding region; and c) 3'-NTR authentic sequences.

On page 4, amend the fourth paragraph as follows:

In WO 99/04008, Purcell et al. disclosed an HCV infectious clone that also contained only the highly conserved 5'-terminal sequence "GCCAGC" (SEQ ID NO. 27).

On pages 4-5, amend the bridging paragraph as follows:

Recently Lohman et al. 1999 (Science 285, 110-113) and Bartenschlager, R. et al., 1993, J. Virol., 67, 3835-3844(in CA 2,303,526, laid-open on October 3, 2000) disclosed a HCV cell culture system where the viral RNA (I377/NS2-3') self-replicates in the transfected cells with such efficiency that the quality of replication can be measured with accuracy and reproducibility. The Lohman and Bartenschlager, R. et al., 1993, J. Virol., 67, 3835-3844 disclosures were the first demonstration of HCV RNA replication in cell culture that was substantiated through direct measurement by Northern blots. This replicon system and sequences disclosed therein highlight once again the conserved 5' sequence "GCCAGC" (SEQ ID NO. 27). A similar observation highlighting the conservation of the 5'NTR was made by Blight et al. 2000 (Science 290, 1972-1974) and WO 01/89364 published on Nov. 29, 2001.

On page 7, under DETAILED DESCRIPTION OF THE DRAWINGS amend the first paragraph as follows:

Figure 1 is a schematic view of the bi-cistronic replicon RNA. The sequence deviations between the I377/NS2-3' replicon from Lohman et al., 1999 Science 285: 110-113 and the

APGK12 replicon are indicated below the replicon. In place of a G nucleotide at the +1 position in the I377/NS2-3'replicon, the APGK12 contains an additional G resulting in GG at the 5' terminus (the first G being counted as position –1). In the linker region between the neo gene and the EMCV IRES sequence two areas deviate from I377/NS2-3': 14 nucleotides (CGCGCCCAGATGTT) (SEQ ID NO. 28) which are not present in I377/NS2/3 are inserted at position 1184 in APGK12; 11 nucleotides (1231-1241) present in I377/NS2-3' are deleted to generate APGK-12. In the NS5B coding region, a T at position 8032 was mutated to C to eliminate a NcoI restriction site.

On page 11, amend the seventh paragraph as follows:

"Restriction endonuclease or restriction enzyme" is an enzyme that has the capacity to recognize a specific base sequence (usually 4, 5 or 6 base pairs in length) in a DNA molecule, and to cleave the DNA molecule at every place where this sequence appears. An example of such an enzyme is *EcoRI*, which recognizes the base sequence G↓AATTC (SEQ ID NO. 29) and cleaves a DNA molecule at this recognition site.
"Restriction fragments" are DNA molecules produced by the digestion of DNA with a restriction endonuclease. Any given genome or DNA segment can be digested by a particular restriction endonuclease into at least two discrete molecules of restriction fragments.

On page 15, amend the second paragraph as follows:

According to the first embodiment of this invention, there is particularly provided a HCV polynucleotide construct comprising:

- a 5'-non translated region (NTR) comprising the sequence ACCAGC (SEQ ID NO. 8) at, or proximal to, its 5'-terminus;
- a HCV polyprotein coding region; and
- a 3'-NTR region.

On page 15, amend the sixth paragraph as follows:

According to the second embodiment, the present invention particularly provides a HCV polynucleotide construct comprising:

- a 5'-NTR region comprising the sequence ACCAGC (SEQ ID NO. 8) at, or proximal to, its 5'-terminus;

- a HCV polyprotein region coding for a HCV polyprotein comprising a G(2042)C or a G(2042)R mutation; and
- a 3'-NTR region.